1-2-02

1656

SN 09/627,753

Case No. 4264C5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Livak et al.

Serial No.: 09/627,753

Filed: July 28, 2000

For: **Hybridization Assay Using Self-Quenching Fluorescence Probe**

Group Art Unit: 1656

Examiner: J. Riley

CERTIFICATE OF EXPRESS MAILING

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RESPONSE UNDER 37 CFR 1.111

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

With reference to the Office action mailed June 22, 2001, reconsideration of the application is respectfully requested. Claims 39-40 are pending.

A Petition for 3-Month Extension of Time is enclosed herewith, extending the time for response to Wednesday, December 26, 2001 (since the Patent Office is closed on December 24th due to an executive order, and on December 25th due to Christmas).

I. Rejection Under 35 U.S.C. 103(a)

Claims 39-40 were rejected as being unpatentable over Heller et al. (EP 229943) in view of Urdea et al. (US 4,775,619). Heller et al. was cited as teaching probes containing donor and

acceptor fluorophores. Urdea was cited as teaching methods for detection of specific sequences employing a solid support. The rejection is respectfully traversed.

The PTO has the burden of establishing *prima facie* obviousness, and can meet this burden "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references" In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claim 39 recites a method for detecting nucleic acid target sequences wherein a sample is contacted with an oligonucleotide probe attached to a solid support under conditions favorable for hybridization. The oligonucleotide probe includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of said reporter molecule. The probe exists in at least one single-stranded conformation when unhybridized to target where the quencher molecule quenches the fluorescence of the reporter molecule, and at least one conformation when hybridized to the target where the fluorescence intensity of the reporter molecule is unquenched, such that the ratio of the fluorescence intensities of the reporter molecule to the quencher molecule when the probe is hybridized to the target is greater than the ratio when the probe is single-stranded. The fluorescence of the reporter molecule is then monitored, wherein an increase in the fluorescence intensity of the reporter molecule indicates the presence of the target sequence.

In the present case, only in hindsight could the present claims have been deemed to be obvious, as there appears to be no teaching or suggestion of the present invention, wherein a probe as recited in claims 39-40 is contacted with a nucleic acid sample and the reporter is monitored, wherein an increase in the fluorescence intensity of the reporter molecule indicates the presence of the target sequence. In the absence of motivation in the cited art to combine the teachings thereof to arrive at the present invention, the claims cannot be considered obvious. Withdrawal of the rejection is therefore respectfully requested.

II. Obviousness Type Double Patenting Rejection

Claims 39-40 were rejected as allegedly being unpatentable over claims in U.S. 5,876,930 and 6,030,787. It is requested that this rejection be held in abeyance until allowable subject matter is indicated by the Examiner.

III. Fee Authorization

Should any extension of time and/or fee be necessary for timely submission of this paper, such extension of time is hereby requested, and the Commissioner is hereby authorized to charge **Deposit Account No. 01-2213**. Any deficiency or overpayment should be charged or credited to this deposit account.

Respectfully submitted,

Date: Dec. 26, 2001

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